DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

April 2, 2015

ABBOTT LABORATORIES
SUSHMA RAO
REGULATORY AFFAIRS PROJECT MANAGER
1921 HURD DRIVE
IRVING TX 75038

Re: K150510
Trade/Device Name: Total Bilirubin
Regulation Number: 21 CFR 862.1110
Regulation Name: Bilirubin (total or direct) test system
Regulatory Class: II
Product Code: CIG, MQM
Dated: March 2, 2015
Received: March 3, 2015

Dear Sushma Rao:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

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For: Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K150510

Device Name
Total Bilirubin

Indications for Use *(Describe)*

The Total Bilirubin assay is used for the quantitation of total bilirubin in human serum or plasma of adults and neonates on the ARCHITECT c8000 System.
Measurement of total bilirubin, an organic compound formed during the normal and abnormal destruction of red blood cells, is used in the diagnosis and treatment of liver, hemolytic, hematological and metabolic disorders, including hepatitis and gall bladder block. A bilirubin (total and unbound) in the neonate test system is a device intended to measure the levels of bilirubin (total and unbound) in the blood (serum) of newborn infants to aid in indicating the risk of bilirubin encephalopathy (kernicterus).

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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k150510

510(k) Summary (Summary of Safety and Effectiveness)

This summary of the 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

1. Applicant Name

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Date Summary prepared: April 2, 2015

2. Device Name

Trade Name: Total Bilirubin
Device Classification: Class II

Classification Name: Total Bilirubin Reagent
Governing Regulation: CFR 862.1110
Product Code: CIG

Classification Name: Bilirubin (total and unbound) in the neonate test system
Governing Regulation: 862.1113
Product Code: MQM

3. Predicate Device

Total Bilirubin, K121985

4. Description of Device

The Total Bilirubin reagent kit contains:

	Number of Bottles × Volume	
Component	**7P32-21**	**7P32-41**
Reagent 1 (R1)	10 × 53 mL	8 × 93 mL
Reagent 2 (R2)	10 × 17 mL	8 × 28 mL
Estimated tests per kit*	2750	3840

* Calculation is based on the minimum reagent fill volume per kit.

Reagent	**Reactive Ingredients**	**Concentration**
Reagent 1	Surfactants	10.57%
	HCl	6.563 g/L
Reagent 2	2, 4-dichloroaniline	0.81 g/L
	HCl	5.563 g/L
	Sodium nitrite	0.345 g/L
	Surfactant	1.96%

Principles of the Procedure

Total (conjugated and unconjugated) bilirubin couples with a diazo reagent in the presence of a surfactant to form azobilirubin. The diazo reaction is accelerated by the addition of surfactant as a solubilizing agent. The increase in absorbance at 548 nm due to azobilirubin is directly proportional to the total bilirubin concentration.

5. Indication for Use

The Total Bilirubin assay is used for the quantitation of total bilirubin in human serum or plasma of adults and neonates on the ARCHITECT c8000 System.
Measurement of total bilirubin, an organic compound formed during the normal and abnormal destruction of red blood cells, is used in the diagnosis and treatment of liver, hemolytic, hematological and metabolic disorders, including hepatitis and gall bladder block. A bilirubin (total and unbound) in the neonate test system is a device intended to

measure the levels of bilirubin (total and unbound) in the blood (serum) of newborn infants to aid in indicating the risk of bilirubin encephalopathy (kernicterus).

6. Comparison of Technological Characteristics

The Total Bilirubin assay is used for the quantitative analysis of total bilirubin in human serum or plasma of adults and neonates on the ARCHITECT *c* 8000 System.

A comparison of the candidate assay (Total Bilirubin) and the predicate assay (K121985) is presented in the table below.

Comparison of Total Bilirubin to Predicate Total Bilirubin Assay on the ARCHITECT *c*8000 Analyzer

Assay Characteristics	Total Bilirubin	Predicate Total Bilirubin Assay (K121985) on the ARCHITECT *c*8000 System
Intended Use	The Total Bilirubin assay is used for the quantitative analysis of total bilirubin in human serum or plasma of adults and neonates on the ARCHITECT *c* 8000 System.	Same
Assay Principle	Total (conjugated and unconjugated) bilirubin couples with a diazo reagent in the presence of a surfactant to form azobilirubin. The diazo reaction is accelerated by the addition of surfactant as a solubilizing agent. The increase in absorbance at 548 nm due to azobilirubin is directly proportional to the total bilirubin concentration.	Same
Detection of Analyte	End-point colorimetric	Same
Samples	Serum or plasma	Same
Assay Range	0.3 to 25.0 mg/dL	0.1 to 25.0 mg/dL
Reference Range - Newborn	Range (mg/dL) Premature Newborn < 24 Hours < 8.0 < 48 Hours < 12.0 3 to 5 Days < 15.0 7 Days < 15.0 Full Term Newborn < 24 Hours < 6.0 < 48 Hours < 10.0 3 to 5 Days < 12.0 7 Days < 10.0	Same
Reference Range - Adult	0.3 to 1.2 mg/dL	0.2 to 1.2 mg/dL
Reagent Formulation	R1: Surfactants 10.57% HCl 6.563 g/L R2: 2,4-dichloroaniline 0.81 g/L HCl 5.563 g/L Sodium nitrite 0.345 g/L Surfactant 1.96%	R1: Surfactants 4.51% HCl 8.204 g/L R2: (Same) 2,4-dichloroaniline 0.81 g/L HCl 5.563 g/L Sodium nitrite 0.345 g/L Surfactant 1.96%

7. Summary of Performance Testing

Limit of Blank (LOB), Limit of Detection (LOD), and Limit of Quantitation (LOQ)

The study was performed based on guidance from the Clinical and Laboratory Standards Institute (CLSI) document EP17-A2. LoB was determined using 4 samples prepared with human serum albumin (zero-analyte samples). LoD and LoQ were determined using low-level analyte samples prepared from human serum albumin and unconjugated bilirubin. A minimum of 2 low-analyte level samples were gravimetrically prepared at each of the following 8 target concentration levels: 0.010, 0.020, 0.040, 0.080, 0.150, 0.300, 0.450, and 0.600 mg/dL. The zero-analyte samples were tested in a minimum of 5 replicates on 5 separate runs. The low-analyte samples were tested in a minimum of 10 replicates on 5 separate runs. Testing was performed over a minimum of 3 days using 2 lots of reagent, 2 lots of commercially available calibrators, and 1 lot of commercially available controls on 3 ARCHITECT *c* 8000 instruments. Each reagent lot was matched with a different lot of calibrator.

LOQ is defined as the lowest concentration at which an assay can meet the total allowable error, which includes bias and imprecision. LOQ is based on 180 results meeting the <10% bias acceptance criteria. Therefore, the LOD is equivalent to LOQ.

The LoQ of the Total Bilirubin assay is 0.174 mg/dL. The LoQ supports the lower end of the measuring interval of 0.3 mg/dL. LoD is 0.174 mg/dL and LoB is 0.102 mg/dL.

Linearity

Linearity was determined based on guidance from National Committee for Clinical Laboratory Standards (NCCLS) document EP6-A. Three combined bilirubin pools were prepared:

- Pool 1: 75% conjugated bilirubin stock / 25% unconjugated bilirubin stock
- Pool 2: 50% conjugated bilirubin stock / 50% unconjugated bilirubin stock
- Pool 3: 25% conjugated bilirubin stock / 75% unconjugated bilirubin stock

A sample set was prepared for each combined bilirubin pool. Each sample set consisted of 12 levels at the following total bilirubin target concentrations: 0.0 (serum), 0.1, 0.5, 2.0, 4.0, 8.0, 12.0, 16.0, 20.0, 22.0, 25.0, and 28.0 mg/dL. Levels 1 through 12 for each

sample set were tested in a random order in a minimum of 4 replicates using 2 lots reagents and 1 lot each of commercially available calibrators and controls on 1 ARCHITECT *c* 8000 instrument. All levels in a sample set were tested in the same run.

The Total Bilirubin assay, was demonstrated to be linear across the measuring interval of 0.3 to 25.0 mg/dL

Within-Laboratory Precision (20-Day)

Precision was evaluated using the following Bio-Rad serum based control materials.

- Level 1: Bio-Rad Lyphochek Unassayed Chemistry Control Level 1
- Level 2: Bio-Rad Lyphochek Unassayed Chemistry Control Level 2
- Level 3: Bio-Rad Liquichek Pediatric Control Level 1
- Level 4: Bio-Rad Liquichek Pediatric Control Level 2

The levels were tested in a minimum of 2 replicates 2 times per day (separated by a minimum of 2 hours) for a total of 20 testing days. Testing was performed using 2 lots of reagents and commercially available calibrators and 1 lot of commercially available controls on 2 ARCHITECT *c* 8000 instruments. During each run, a given reagent lot/calibrator lot combination was randomly tested. Therefore, for each instrument, the 20 days of testing included up to 4 instrument/reagent lot combinations.

The analysis was performed based on guidance from National Committee for Clinical Laboratory Standards (NCCLS) document EP5-A2.

Results Table:

			Within Run		Total	
Sample	N	Mean (mg/dL)	SD (mg/dL)	%CV	SD (mg/dL)	%CV
1	80	0.87	0.010	1.2	0.018	2.1
2	80	4.53	0.034	0.8	0.057	1.3
3	80	6.42	0.041	0.6	0.066	1.0
4	80	16.85	0.115	0.7	0.204	1.2

			Within Run		Total	
Sample	N	Mean (µmol/L)	SD (µmol/L)	%CV	SD (µmol/L)	%CV
1	80	14.90	0.17	1.2	0.31	2.1
2	80	77.57	0.58	0.8	0.97	1.3
3	80	109.93	0.70	0.6	1.13	1.0
4	80	288.53	1.97	0.7	3.49	1.2

Interference

The interference study was performed based on guidance from CLSI document EP7-A2. Interference effects were assessed by dose response and paired difference methods at two total bilirubin concnetrations (15mg/dL and 1.2 mg/dL, respectively). A bias of > 10%, or > 0.2 mg/dL (> 3.4 µmol/L) for bilirubin concentrations ≤ 2.0 mg/dL is considered significant interference.

Results Tables: (Conventional and International Units)

Interferent		Bilirubin		
Interfering Substance	Interferent Concentration	Control (mg/dL)	Observed (mg/dL)	Diff (%)
Hemoglobin	2000 mg/dL	1.0	-0.1	-9.8
	2000 mg/dL	13.4	-0.4	-3.0
Intralipid	1000 mg/dL	1.0	0.0	-0.6
	1000 mg/dL	13.4	-0.1	-0.6
Indican	0.125 mmol/L	0.9	0.2	26.7
	0.25 mmol/L	14.7	0.5	3.2

Interferent		Bilirubin		
Interfering Substance	Interferent Concentration	Control (µmol/L)	Observed (µmol/L)	Diff (%)
Hemoglobin	20 g/L	17.1	-1.7	-9.8
	20 g/L	229.1	-6.8	-3.0
Intralipid	10 g/L	17.1	0.0	-0.6
	10 g/L	229.1	-1.7	-0.6
Indican	0.125 mmol/L	15.4	3.4	26.7
	0.25 mmol/L	251.4	8.6	3.2

Indican, at concentrations > 0.125 mmol/L, interferes with the assay in samples with bilirubin levels at 1.2 mg/dL.

Method Comparison

The study was performed based on guidance from CLSI document EP09-A2-IR. A total of 124 adult patient specimens and 64 neonatal patient specimens were evaluated with the candidate Total Bilirubin assay and the predicate Total Bilirubin (k121985) assay. A total of 4 adult and 4 neonate patient samples were spiked. Each sample was tested using 2 lots each of the candidate Total Bilirubin assay and the predicate Total Bilirubin (k121985) reagents and 1 lot each of commercially available calibrators and controls. Testing was performed in duplicate on the candidate Total Bilirubin assay and in duplicate on the predicate Total Bilirubin assay over 5 separate days on 1 ARCHITECT *c* 8000 System. Passing-Bablok regression results based on singlet test results from a representative reagent lot are summarized below:

Adult Population Representative Data

N	Slope	Intercept	Correlation Coefficient	Range (mg/dL)
118	0.99	-0.09	0.9994	0.3 to 24.8

Neonate Population Representative Data

N	Slope	Intercept	Correlation Coefficient	Range (mg/dL)
54	0.96	0.01	0.9982	0.3 to 24.3

Reference Range

The study was performed based on guidance from CLSI document EP28-A3c. Fresh, adult patient serum samples from a clinically healthy population of non-distinguished adult male and female patients were obtained. The samples were stored at 2 to 8°C and protected from light when not in use. The samples were up to 3 days old when received at the testing site. The samples were tested on the day they were received at the testing site. The samples were tested in a replicate of 1 using 1 lot of reagents and 1 lot each of commercially available calibrators and controls on 1 ARCHITECT *c* 8000 instrument.

The Total Bilirubin assay, which had a total of 4 of 40 samples (10%) outside the reference range (all out-of-range samples were < 0.3 mg/dL).

The reference range was determined to be 0.3 mg/dL to 1.2 mg/dL.

Automated Dilution Protocol versus Manual Dilution Procedure

Fresh serum specimens were obtained and, if necessary, pooled to create test samples at the following target total bilirubin concentrations: 34, 32, 30, 28, 26, and 24 mg/dL. The samples were divided into 3 portions. One portion of each sample was tested using the 1:5 and 1:10 autodilution protocols. Two portions were manually diluted using 0.85% saline solution, one at 1:5 and the other at 1:10. All portions were tested in replicates of

6 in the same run as the autodiluted samples using 1 lot of reagents on one ARCHITECT *c* 8000 System.

The Total Bilirubin assay met the acceptance criteria of a difference between the autodilution mean concentration and the manual dilution mean concentration of ≤ 10% bias. For Total Bilirubin samples greater than 25 mg/dL, either the System Automated Dilution protocol or Manual Dilution protocol can be performed.

Specimen Tube Type (Matrix Equivalence)

The study was performed based on guidance from CLSI document EP9-A3 and CLSI document GP34-A. The study control tube type was the serum plastic tube. The following tubes types were under evaluation: serum glass, serum with gel separator, K_2 EDTA plasma (without gel separator), lithium heparin plasma (without gel separator), lithium heparin plasma with gel separator, and sodium heparin plasma (without gel separator). Fresh or frozen sample sets were obtained that included the control tube type and at least 1 tube type under evaluation. Each tube type under evaluation was assessed using a minimum of 40 samples from adult subjects. The sample sets spanned the assay's measuring interval. All samples were tested in replicates of 6 using 1 lot each of reagents and commercially available calibrators and controls on 1 ARCHITECT *c* 8000 System. All samples collected from the same subject were tested in the same run.

Deming linear regression analysis was performed using the first set of results obtained. Results summarized below demonstrated that the following blood collection tube types are acceptable for use with the Total Bilirubin assay:

Tube Type	N	Slope	Intercept	Correlation Coefficient
Serum (glass)	41	0.96	0.06	0.9990
Serum Separator Tube (SST)	40	1.00	0.00	0.9996
Ethylenediaminetetraacetic Acid (EDTA)	39	1.00	-0.01	0.9990
Lithium Heparin	40	1.01	0.02	0.9994
Lithium Heparin Plasma Separator Tube (PST)	40	0.96	0.05	0.9992
Sodium Heparin	39	0.98	0.03	0.9996

Tube type limitation: Tubes containing sodium flouride/potassium oxalate are not recommended due to the potential for hemolysis.

8. Conclusion Drawn from Performance Testing

The results presented in this 510(k) premarket notification demonstrate that the candidate Total Bilirubin assay performance is substantially equivalent to the predicate assay (Total Bilirubin, K121985).